

The University of Chicago

THE ANOMALOUS ROTATIONS OF ALKALOID SALTS

A PART OF A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
1935

By
D. WARREN STANGER

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The author is indebted to Professor M. S. Kharasch and Dr. James K. Senior for advice and assistance in this work, and to the Eli Lilly and Company for the grant of a fellowship.

I. THE ANOMALOUS ROTATIONS OF ALKALOID SALTS

Kuhn's Theory of "Asymmetric Rearrangement of the First Type"

The following investigation was undertaken to test the validity of Kuhn's hypothesis for "asymmetric rearrangement of the first type."¹

Kuhn was led to this idea by the following considerations. One of the first inferences drawn from the theory of electrolytic dissociation was that in dilute solutions of electrolytes the dissociated ions should act independently of one another, and their effect on the physical properties of the solution should be additive. This inference was early tested on the specific gravities and refractive indices of solutions of strong electrolytes; it was found to be correct to a satisfactory order of approximation. Application of the same idea to solutions of electrolytes in which one and only one ion is optically active leads at once to the conclusion that, if such solutions are sufficiently dilute, the rotations should be independent of the optically inactive ions present. For example, all the salts of a given optically active monacid base at low concentrations and under the same physical conditions should show the same rotation. Hädrich² tested out this idea in water solution and found it to be correct. Later the work was extended to certain non-aqueous solutions, principally those in alcohol.³

¹Kuhn, Ber., 65, 49 (1932).

²Hädrich, Z. Physik. Chem., 12, 476 (1893).

³Guye and Rossi, Bull. Soc. Chim., (3), 13, 464 (1895).

Here also the theory was found to work fairly well. Thus there arose the idea of a "normal" rotation in dilute solution for all the salts formed by an optically active base with optically inactive acids. If the rotation of any such salt were found to deviate very widely from this norm, the rotation in question might properly be called "anomalous."

¹Kuhn in his investigation of the quinine and cinchonidine salts of 4,4'-dinitrodiphenic acid noticed such "anomalous" rotations. The specific rotation of the quinine salt in chloroform, $(\alpha)_D^{22} = 110^\circ$, is almost as positive as the specific rotation of quinine in the same solvent, $(\alpha)_D = -117^\circ$, is negative. The salt of the levorotatory alkaloid, cinchonidine, is likewise highly dextrorotatory. In spite of these facts the 4,4'-dinitrodiphenic acid liberated from these alkaloid salts is inactive. To account for these anomalies and those reported by Pfeiffer and Quehl² for complex zinc salts of optically active acids, Kuhn devised his theory of "asymmetric rearrangement of the first type."

It had long been known that if a pair of enantiomorphs is very easily racemized, addition of a compound-forming dissymmetric reagent to a 50-50 mixture of the two forms frequently results in the precipitation of the entire substance as one optically active form. If the dissymmetric precipitating reagent is then removed, this one form rapidly racemizes - a process which evidences itself by a mutarotation. Such behavior had been observed in methyl-ethyl-n-propyl-tin-d-bromecamphorsulphonate,³ I, the oxime of cyclohexanone-4-carboxylic acid,⁴ II, and hydrocarbostyryl-

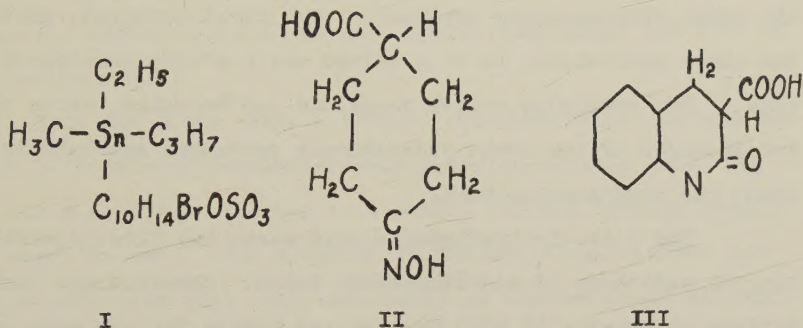
¹Kuhn and Albrecht, Ann., **455**, 272 (1927).

²Pfeiffer and Quehl, Ber., **64**, 2667 (1931).

³Pope and Peachey, Proc. Chem. Soc., **16**, 116 (1900).

⁴Mills and Bain, J. Chem. Soc., **97**, 1866 (1910).

β-carboxylic acid,¹ III.



The sort of activation just described was called by Kuhn "asymmetric rearrangement of the second type." He assumed further that in some compounds the racemization which follows the removal of the dissymmetric reagent is so rapid that the mutarotation is over before it can be observed. Such a compound in the pure form would never exhibit optical activity, but, if it were an acid, dilute solutions of its salts with an optically active base would not show the rotation "normal" for the salts of the base in question. The divergence of the rotation would be due to the optical activity of the acid ion "dissymmetrized by the optically active base. Such divergences Kuhn attributed to "asymmetric rearrangement of the first type."

This idea is easily applicable to certain acids derived from diphenyl, e.g., the 4,4'-dinitrodiphenic acid, which Kuhn had under investigation. Theoretical considerations impose the following conditions for the existence of enantiomorphic forms of a diphenyl derivative: (1) The substituents must be so placed that neither phenyl ring retains a plane of symmetry. (2) The groups in the 2,2',6, and 6' positions must restrict the free

¹Leuchs, Ber., 54, 830 (1921).

rotation of the two nuclei about their common axis and prevent the rings from becoming coplanar. The first compound, meeting the above conditions, to be resolved was 6,6'-dinitrodiphenic acid.¹ The optically active forms did not racemize, since the interference of the ortho substituents prevented any rotation about the interannular bond.

The 4,4'-dinitrodiphenic acid meets the first condition² for the existence of enantiomorphic forms. Christie and Kenner's failure to resolve it with brucine and Kuhn's failure with quinine were accepted as evidence that it does not meet the second condition. However, the anomalous rotation of the quinine and cinchonidine salts was considered by Kuhn as sufficient evidence that he was dealing with an induced dissymmetric form of the acid - in other words, that he had realized an "asymmetric rearrangement of the first type." This argument would be greatly weakened if the same sort of anomalous rotation were found for a quinine salt, the acid ion of which could not exist in enantiomorphic forms.

Other workers have brought to light further examples of anomalous rotations of salts.³ Bell and Robinson noted that the quinine salt of 4-nitrodiphenic acid was strongly dextrorotatory in chloroform, but that the liberated acid was inactive. They suggested that:

The difference in rotatory power may be attributed to: (a) resolution of the alkaloidal salt; (b) admixture of acid and normal quinine salts and quinine; (c) difference in the number of molecules of solvent of crystallization; or (d) possible presence of 6-nitro- and 4,4'-dinitrodiphenic acid as impurities.

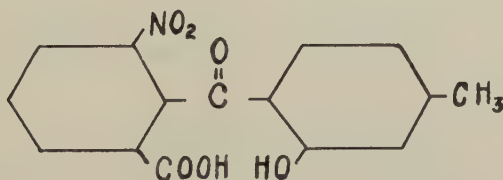
¹Christie and Kenner, J. Chem. Soc., 121, 614 (1922).

²Ibid.

³Bell and Robinson, J. Chem. Soc., 1927, 2234.

Haworth¹ referred to Kuhn's work and assumed that 4,4'-di-nitrodiphenic acid, when combined with alkaloids undergoes an "asymmetric transformation" to give almost completely the salt of one enantiomorph.

Hyde and Adams² made a similar observation on the brucine salt of 2-(2-hydroxy-4-methyl-benzoyl)-3-nitrobenzoic acid, IV, which has a positive rotation in acetone, whereas brucine itself has a negative one. They referred to Haworth's conclusions and made the criticism that they were based on too few facts and did not take into consideration the work of Hilditch on alkaloid salts.



IV

It was not, however, until Pfeiffer and Quehl³ reported on their work in 1931 that Kuhn announced his hypothesis on types of asymmetric rearrangement. These workers observed a "new effect" in the complex zinc salts of optically active acids, (ZnY₃)X₂, where Y is a diacid organic base such as ethylene diamine, α , α -dipyridyl, or α -phenanthroline, and X is a univalent optically active acid ion. The rotatory power of these salts was found to deviate sharply from that of the corresponding zinc salts, ZnX₂.

¹W. N. Haworth, "Annual Reports on the Progress of Chemistry for 1927," Gurney and Jackson, London, 1928, v. 24, p. 101.

²Hyde and Adams, J. Am. Chem. Soc., **50**, 2499 (1928).

³Loc. cit.

They explained this discrepancy by assuming that the active ion of the acid had induced optical activity in the complex zinc ion.

In 1932, Kramer¹ and Lesslie and Turner² made independent observations of the anomalous rotation of quinine diphenate. Not, however, until the present investigation had been practically finished, did Lesslie and Turner³ report in detail on their work with diphenic acid in substantiation of Kuhn's hypothesis of "asymmetric rearrangement of the first type." They conclude:

Assuming (1) that the salt groups in position 2 and 2' are sufficiently large to collide with the 6' and 6- positions (C or H), (2) that in the solvent used there is only partial ionic or thermal dissociation, and (3) that the free acid and the once or twice ionized acid are capable of unrestricted rotation, it is clear that asymmetric transformation could and should occur, even without separation of any of the solid salt, since the quinine d- and l-salts will almost certainly have different stabilities from the point of view of their ionic or thermal dissociation.

Upon the basis of the above assumptions as to the nature of asymmetric rearrangement, Lesslie and Turner inferred that a decrease in ionization should increase, and increase in ionization should decrease, the specific rotation of quinine diphenate. These two predictions were confirmed. By increasing the concentration of the salt in alcohol-chloroform mixture, the specific rotation was increased; by using as solvent alcohol-water mixtures containing increasing percentages of water, the specific rotation was decreased. These same authors further observed the Kuhn effect, not only in the dextrorotation of the diphenates of the levorotatory alkaloids, quinine, dihydroquinine, and cinchonidine, but also in the levorotation of the diphenates of the dextrorotatory alkaloids, quinine and cinchonine. In addition, they observed a slight mutarotation, that is, the rotation increased

¹Kramer, Unpublished Master's Thesis, University of Chicago 1932.

²Lesslie and Turner, J. Soc. Chem. Ind., 51, 493 (1932).

³Idem, J. Chem. Soc., 1934, 347.

slightly with time. This change they regarded as the last stage of the rapid process of asymmetric induction. In the course of the present investigation a careful repetition of Lesslie and Turner's work on quinine diphenate failed to reveal any mutarotation.

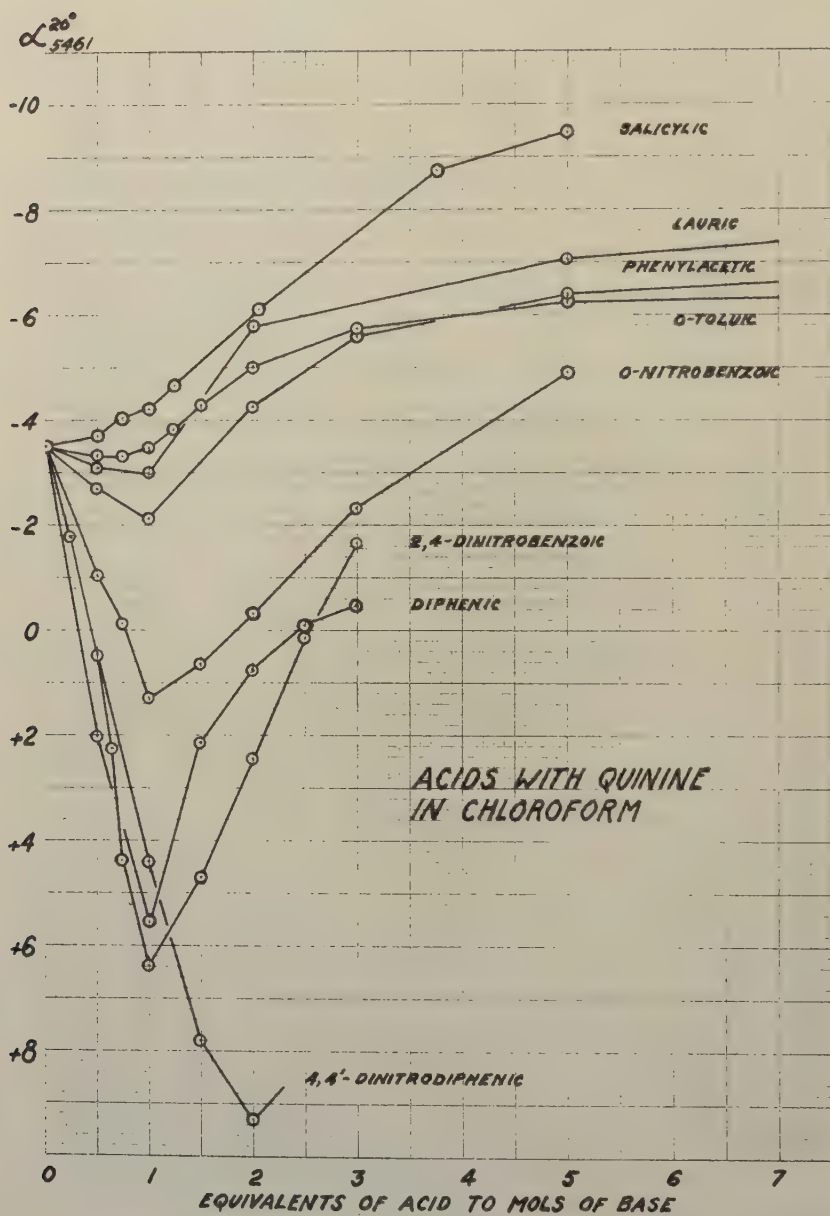
The hypothesis of Kuhn departs from classic chemical practice by setting up the new principle that isomer numbers can be determined from anomalies in the optical rotations of solutions. To accept this important innovation without careful investigation seemed most unwise - hence the present study was undertaken. The method proposed was to observe the changes in the optical activity of a fixed quantity of optically active base as the amount of acid per mole of base was varied. Since quinine and chloroform had been used in Kuhn's work on the anomalous rotation of the 4,4'-dinitrodiphenate, this combination was employed to study the effects of varying amounts of organic acids. The results are shown graphically. The angular rotations are plotted as ordinates; the ratios of acid to base as the abscissae.

Study of a representative selection of curves (shown in Figure 1), leads to the following conclusions:

1. There is no apparent justification for calling any one of these widely divergent curves normal or anomalous.

2. Without the assumption that acids like 2,4-dinitrobenzoic can be dissymmetrized (which is a radical departure from classic stereochemistry), asymmetric rearrangement of an acid is not demonstrated by anomalous rotation of its quinine salt in chloroform.

Since quinine is a diacid base, the question was raised as to the behavior of a monacid base under the same conditions. Morphine was chosen for the test. This change necessitated a



change of solvent as well, since morphine and its salts are not sufficiently soluble in chloroform. Cellosolve, the monoethyl ether of ethylene glycol, was selected, and two series of experiments, one on morphine, the other on quinine, were run with a representative group of acids.

The results of these experiments are shown in Figs.7 and 8. The conclusions drawn are:

1. With morphine and cellosolve no anomalous curves are obtained even with those acids which, on the basis of the Kuhn hypothesis, might be "dissymmetrized."

2. In certain solvents, such as cellosolve, anomalous rotations may be demonstrated for diphenic acid itself and for derivatives with substituents in positions other than 6 and 6' provided the proper base is chosen, quinine, not morphine.

Causes of the Anomalous Rotations Shown by Certain Salts of the Quinine Alkaloids

The results of the investigation of the Kuhn hypothesis served as a stimulus to evaluate some of the factors which influence the rotation of salts of optically active bases with optically inactive acids.

The known factors which influence the rotation of solutions of a given solute are as follows:

1. Temperature of the solution.
2. Length of the polariscope tube.
3. Wave length of the light used.
4. Concentration of the solution.
5. Nature of the solvent.

The first four factors are easily subject to laboratory control, but it has been difficult to determine the tendency of the solvent to solvate or dissociate single molecules of the solute or to

break up associated aggregates of these molecules.

¹
In the case of ionization of the solute, H¹drich and
²Walden conclude that: The optical rotation of electrolytes in water solution is dependent on the number of optically active ions and at the most complete dissociation possible, the following statements hold:

1. The rotatory power of salts is independent of the inactive ion.

2. The molecular rotation of binary electrolytes with two optically active ions is equal to the algebraic sum of the molecular rotations of the anions and cations.

³
Rule has attempted to deduce the effect of the solvent from its dipole moment. In general he has found good qualitative agreement between the increase in the dipole moment of the solvent and the decrease in specific rotation of the solution. He concludes that:

In general the rotatory power most characteristic of an optically active solute is exhibited when the substance is dissolved in a non-polar solvent such as benzene or carbon tetrachloride. In aliphatic hydrocarbons like hexane there may be a tendency even at high dilutions for the active compound to exist in the associated state, with a consequent modification of the rotatory power. Solvents containing polar substituents, on the other hand, may affect the rotation by themselves entering into combination or dipole association with the solute. In the latter case, the influence of monosubstituted derivatives of the same parent hydrocarbon tends to be related to the dipole moments of the solvents.

In the work here reported the first factor to be varied was the acid; the base, quinine, and the solvent, chloroform, were held unchanged. The following statements summarize the conclusions drawn from the curves in Figures 2, 3, 4, 5, and 6.

¹Loc. cit.

²Walden, Z. Physik. Chem., 15, 196 (1894).

³Rule and McLean, J. Chem. Soc., 1932, 1415.

Monobasic Acids

1. Aliphatic and halogen or phenyl substituted aliphatic acids.

- (a) Each curve has a minimum, that is, a rotation more positive than that for quinine where the molar ratio of acid to quinine is one.
- (b) On addition of sufficient excess of acid a rotation more negative than that of quinine is attained, and there is a tendency for this rotation to become constant at high acid concentrations.
- (c) Unsaturation in the acid gives a more pronounced minimum; that for crotonic acid is more marked than those for the saturated aliphatic acids, and that for cinnamic acid more marked than those for the phenyl substituted aliphatic acids.

2. o-Substituted benzoic acids.

With the exception of o-nitrobenzoic acid, an acid of this class does not give a minimum; that is, at all concentrations the rotation is more negative than that of quinine. o-Toluic acid may be looked upon as a transitional case, since it shows a slight minimum but not at the one to one mole ratio.

3. m- and p-Substituted benzoic acids.

- (a) Each curve shows a minimum as in 1-(a), but generally the minimum rotation is much more positive; in many cases it is actually positive in sign.
- (b) There is a tendency toward constant rotation at higher acid concentrations but this tendency is not as clearly marked as in 1-(b), because of the limited solubility of the acids.

Monobasic Acids (Cont.)

4. Di- and tri-substituted benzoic acids.

The minimum rotations for these acids are the most positive of all for the monobasic acids.

Dibasic Acids

1. Aliphatic acids.

- (a) There is no minimum except in the case of adipic and oxalic acids.

2. Aromatic acids.

- (a) Phthalic acid shows a minimum.
- (b) Diphenic acid shows a minimum at a ratio of one equivalent of acid to one mole of base.
- (c) 4,4'-Dinitrodiphenic acid shows a pronounced minimum, but at a ratio of two equivalents of acid to one mole of quinine.

To simplify the problem, as explained in the first section, the monacid base morphine was chosen to replace the diacid quinine. Hence it was necessary to obtain two new sets of curves because both bases had to be investigated in cellosolve.

The conclusions drawn from Figures 7 and 8 are:

Diacid Base, Quinine, in Cellosolve

1. All acids, with the exception of those listed under 2 below, cause only a slight change in the rotation of quinine. Beyond the ratio of one equivalent of acid to one mole of quinine, rotation is independent of concentration.
2. Diphenic and 4,4'-dinitrodiphenic acids each exhibit a minimum at a ratio of one equivalent of acid to one mole of quinine.

Monacid Base, Morphine, in Cellosolve

1. Aromatic acids tend to give rotations lower than that of pure quinine; there is also a tendency towards constant

rotation with increase in acid concentration.

2. There is no detectible difference between the diphenic acids and the other acids.

As the alkaloids, quinine and morphine, are relatively complex molecules, β -naphthol-phenyl-methylamine, V, $(C_6H_5)-\alpha-(\beta-C_{10}H_6OH)CH-NH_2$, was chosen as a simpler base. This molecule containing only one asymmetric carbon atom had been prepared and resolved by Betti.¹ As this base is hydrolytically not very stable, the analogous but more stable compound, β -naphthol- β -phenylethyl-methylamine, VI, $(C_6H_5CH_2CH_2)-\alpha-(\beta-C_{10}H_6OH) \cdot CH-NH_2$, first described by Kharasch and Howard², and hereafter called Howard's base, was also used. In order to approximate a dibasic alkaloid, the optically active forms of each of these two bases were condensed with p-dimethylaminobenzaldehyde. Reduction of these condensates was also attempted so as to secure maximum basicity. The effort was successful with the condensation product of d-Betti's base, but no reduction without racemization could be effected with the optically active condensation product of Howard's base.

The curves obtained by the use of Betti's base and its derivatives in chloroform or cellosolve are without significance, because of the rapid racemization of the base. The curves obtained with Howard's base and cellosolve show the same relations as those for morphine and cellosolve.

It was decided to turn back to the naturally occurring

¹Betti, *Gazz. Chim. Ital.*, **31**, I, 385 (1901); **36**, II, 392 (1906). Marvel and Hiers, "Organic Syntheses," John Wiley and Sons, New York, 1932, Collective Vol. I, p. 372.

²Kharasch and Howard, *J. Am. Chem. Soc.*, **56**, 1370 (1934).

bases. Brucine was examined, but, as the behavior of this substance differed from that of quinine, it was thought that the investigation of quinine derivatives might shed more light on the problem than the study of other bases. For this purpose hydroquinine, acetylquinine, benzoylquinine, and quinine chloride were used.

The results of the work on these bases are shown in Figures 9, 10 and 11. The curves for brucine in chloroform are of the same type as those for Howard's base or morphine in cello-solve. The curves for hydroquinine in chloroform show no appreciable difference from those for quinine itself. The curves for acetylquinine, benzoylquinine, and quinine chloride in chloroform show no relationship to those of quinine or hydroquinine in the same solvent. From this it may be concluded that the anomalous behavior of quinine salts is related to the presence of the free hydroxyl group in the quinine molecule.

¹ Experimental Part

Acids.- To insure the purity of the acids used, those whose melting points deviated by two degrees or more from the accepted values were recrystallized until their melting points were brought within this limit of deviation. The following acids, not otherwise available, were prepared:

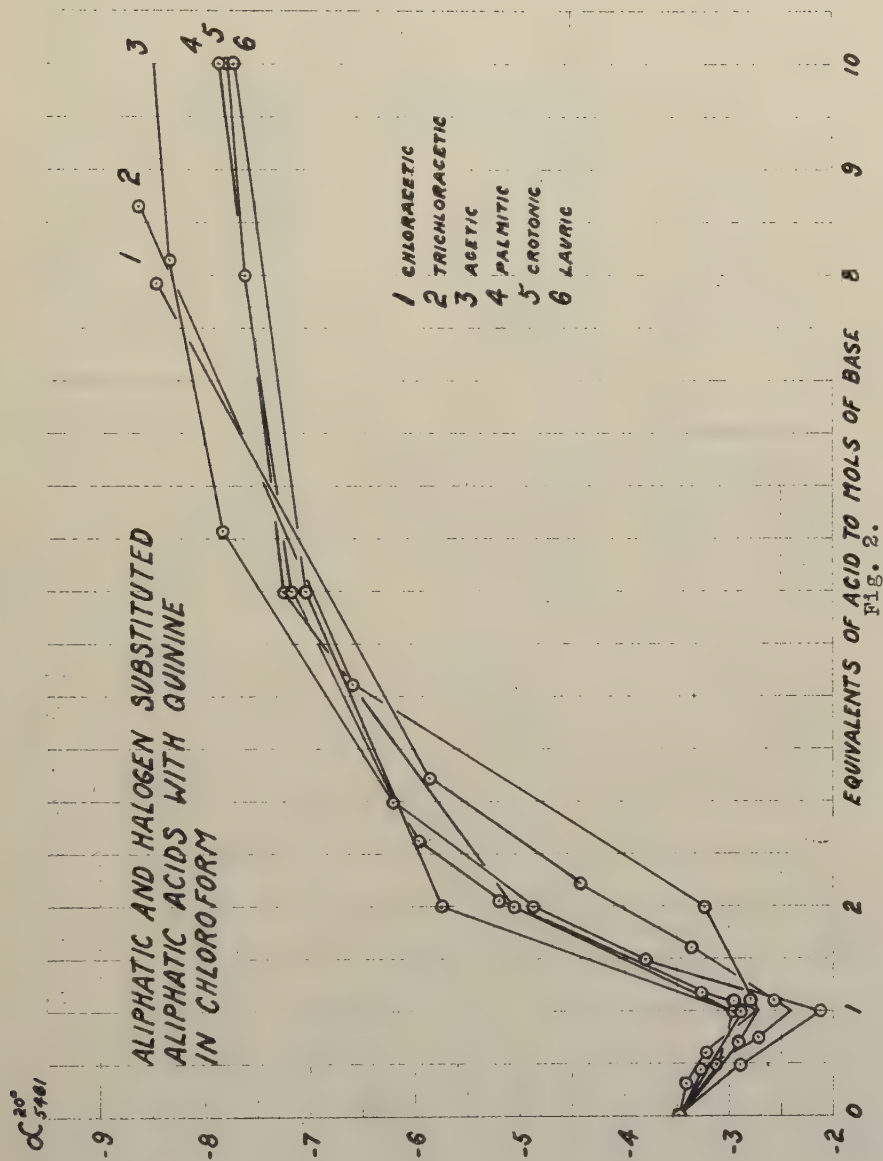
o-Phenylbenzoic acid was prepared from fluorenone according to the method of Graebe and Rateanu.² For further purification the acid was recrystallized from hot 40% alcohol.

3,3'-Diphenyldicarboxylic acid was prepared from m-iodo-benzoic acid methyl ester by the Ullmann³ synthesis.

¹J. A. Chenicek co-operated in carrying out these experiments and a portion of his results are included here.

²Graebe and Rateanu, Ann., 279, 260 (1894).

³Ullmann and Lowenthal, Ann., 332, 71 (1904).



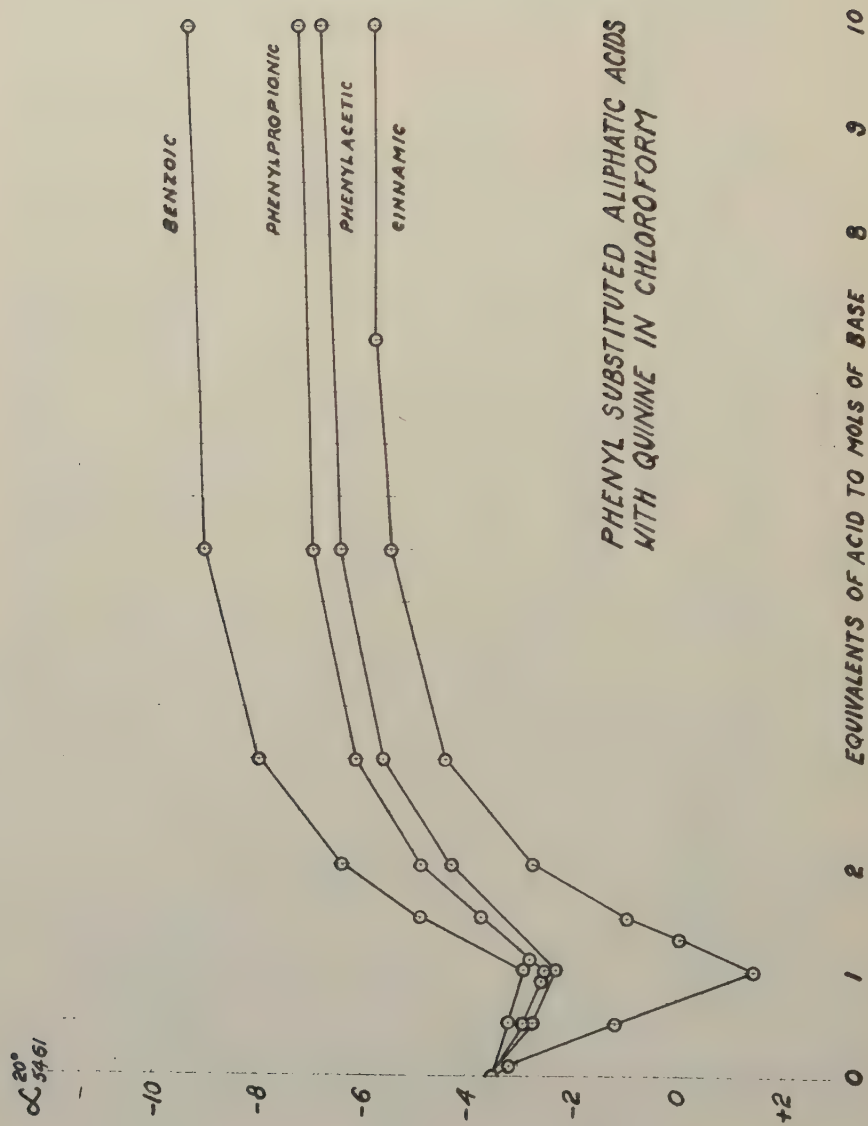


Fig. 3.

α_{5461}^{20}

O-SUBSTITUTED BENZOIC ACIDS
WITH QUININE IN CHLOROFORM

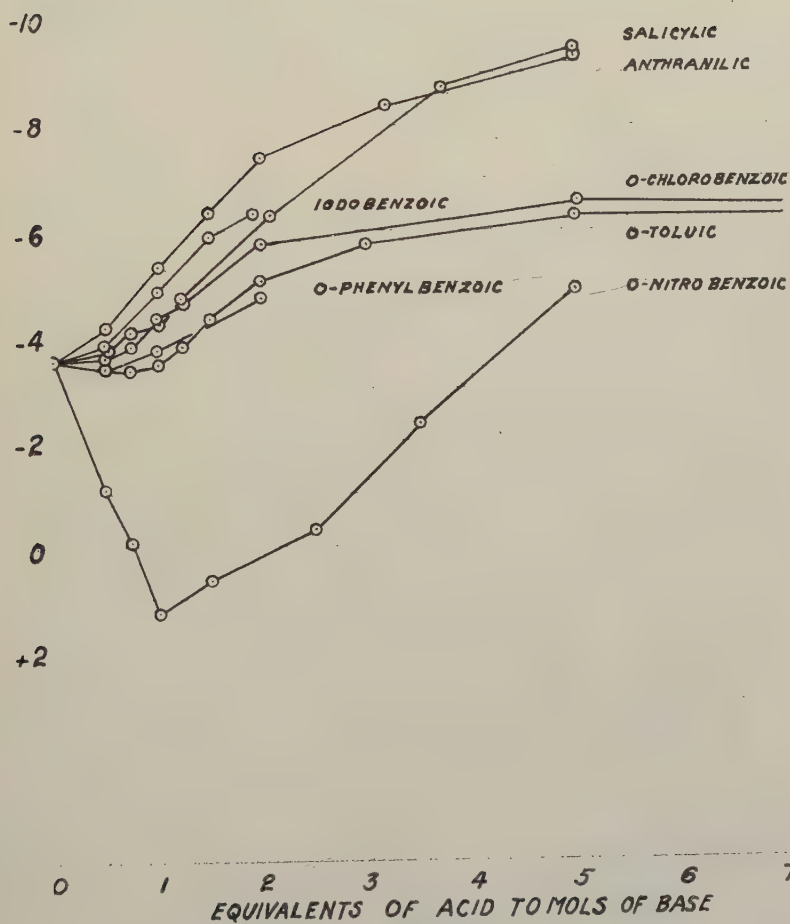


Fig. 4

α^{20°
5461

M-AND P-MONOSUBSTITUTED AND DI-AND TRI-SUBSTITUTED BENZOIC ACIDS WITH QUININE IN CHLOROFORM

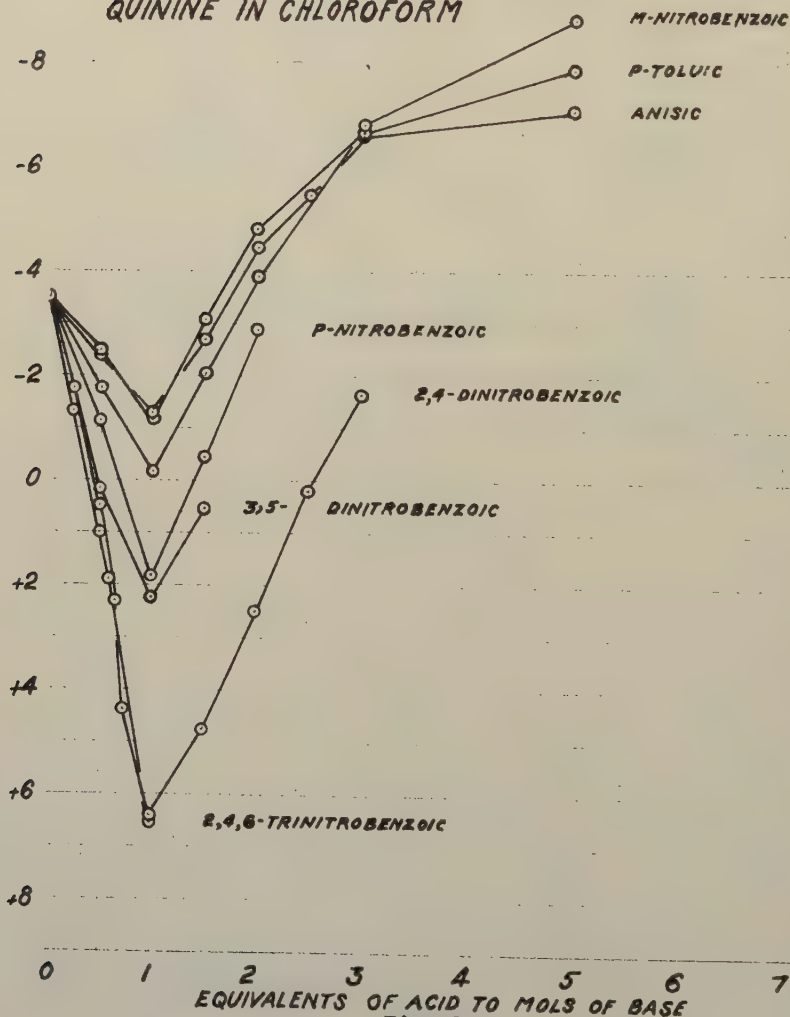
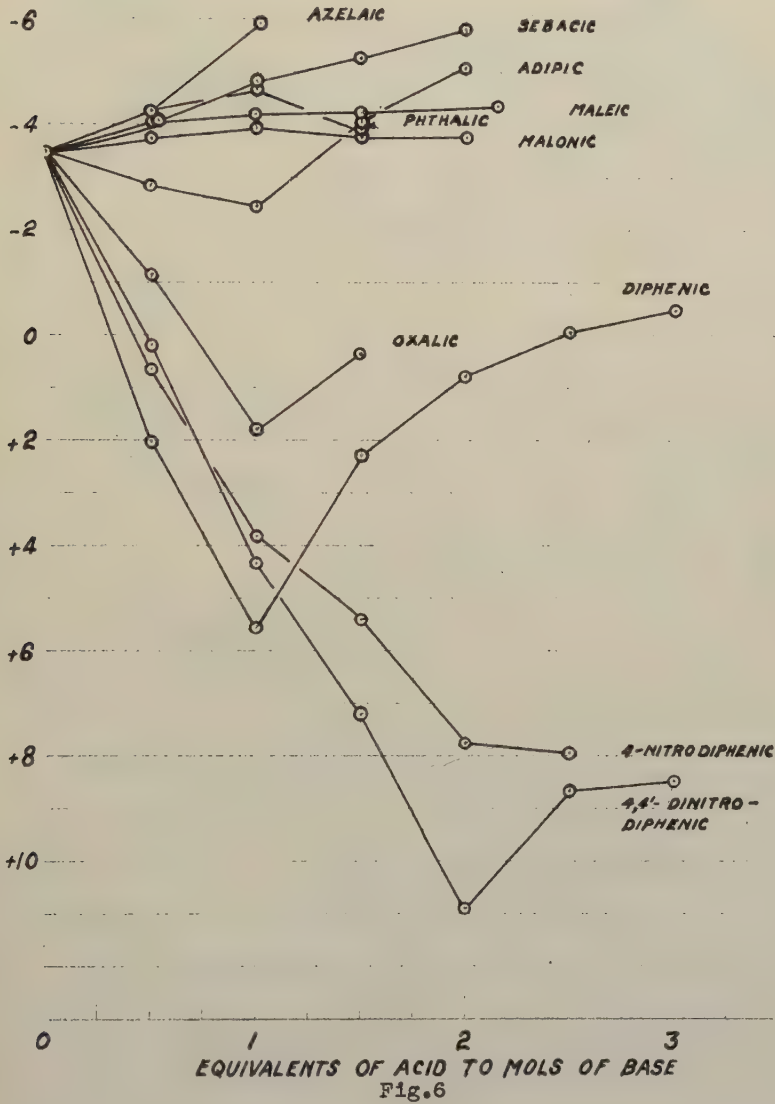


Fig. 5

α_{20}^{20}
5461

DIBASIC ACIDS WITH QUININE IN CHLOROFORM



$\alpha_{5461}^{20^\circ}$

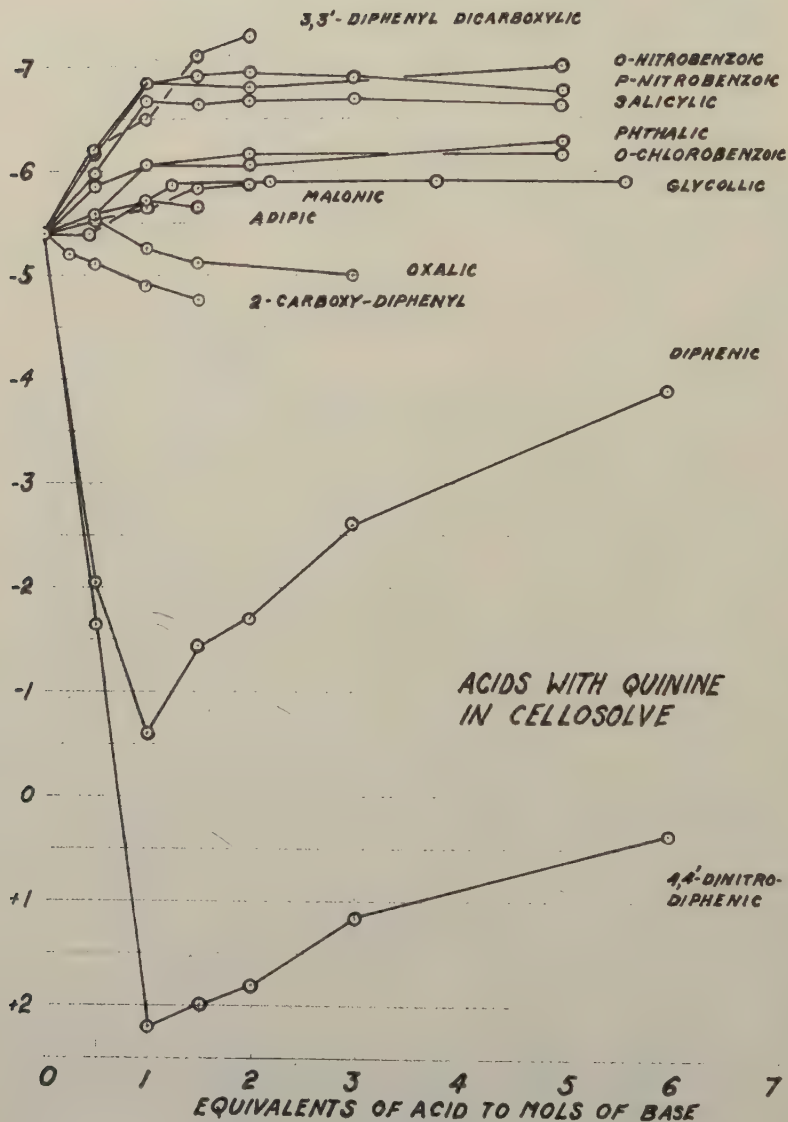
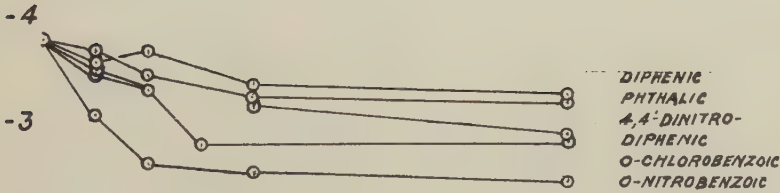
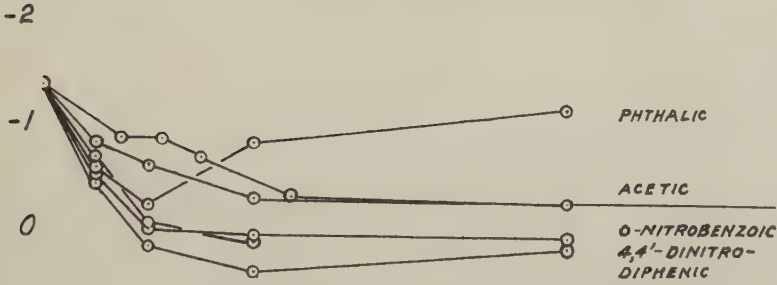


Fig. 7.

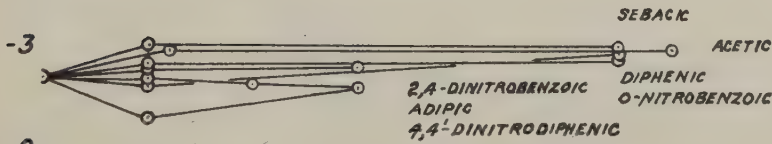
$\alpha_{5461}^{20^\circ}$



ACIDS WITH MORPHINE
IN CELLOSOLVE



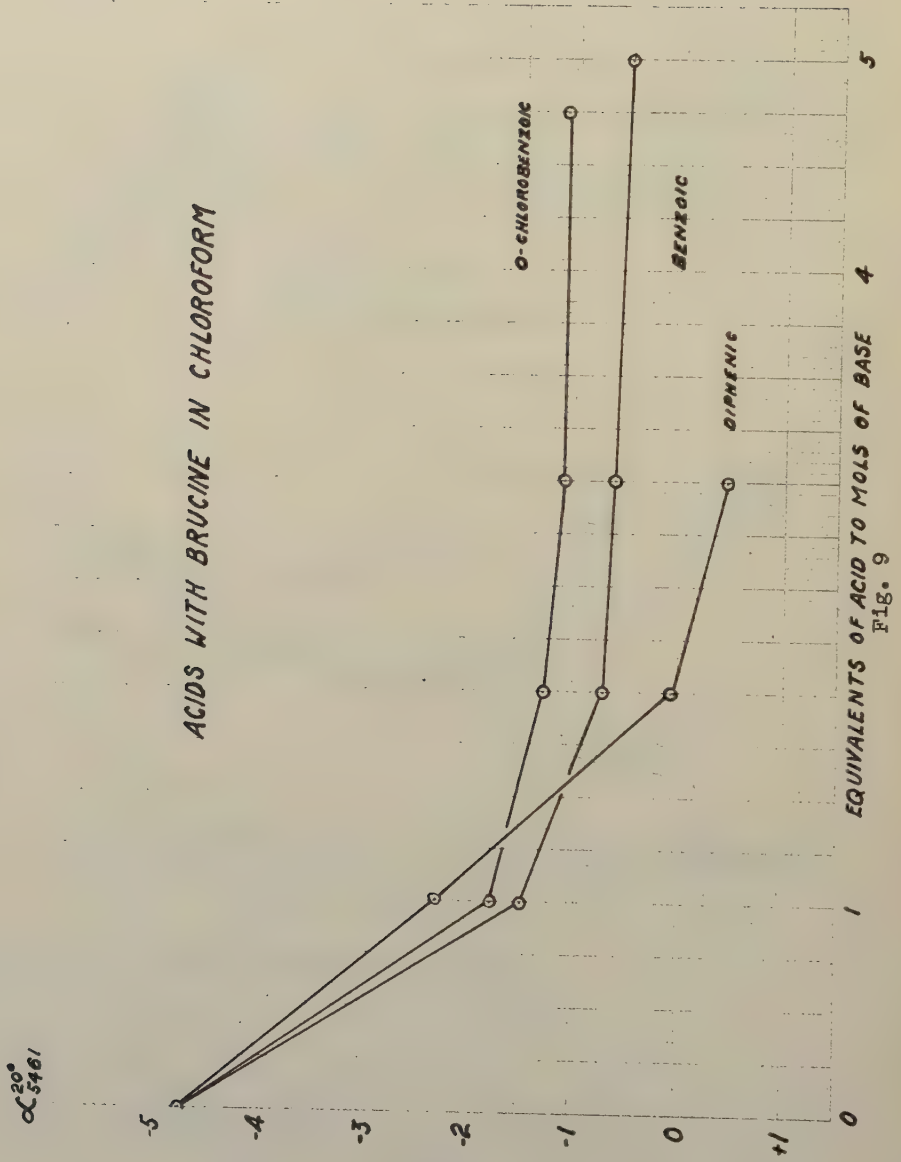
ACIDS WITH HOWARD'S BASE
IN CELLOSOLVE



ACIDS WITH BETT'S BASE
IN CELLOSOLVE

0 1 2 3 4 5 6 7
EQUIVALENTS OF ACID TO MOLs OF BASE

Fig. 8



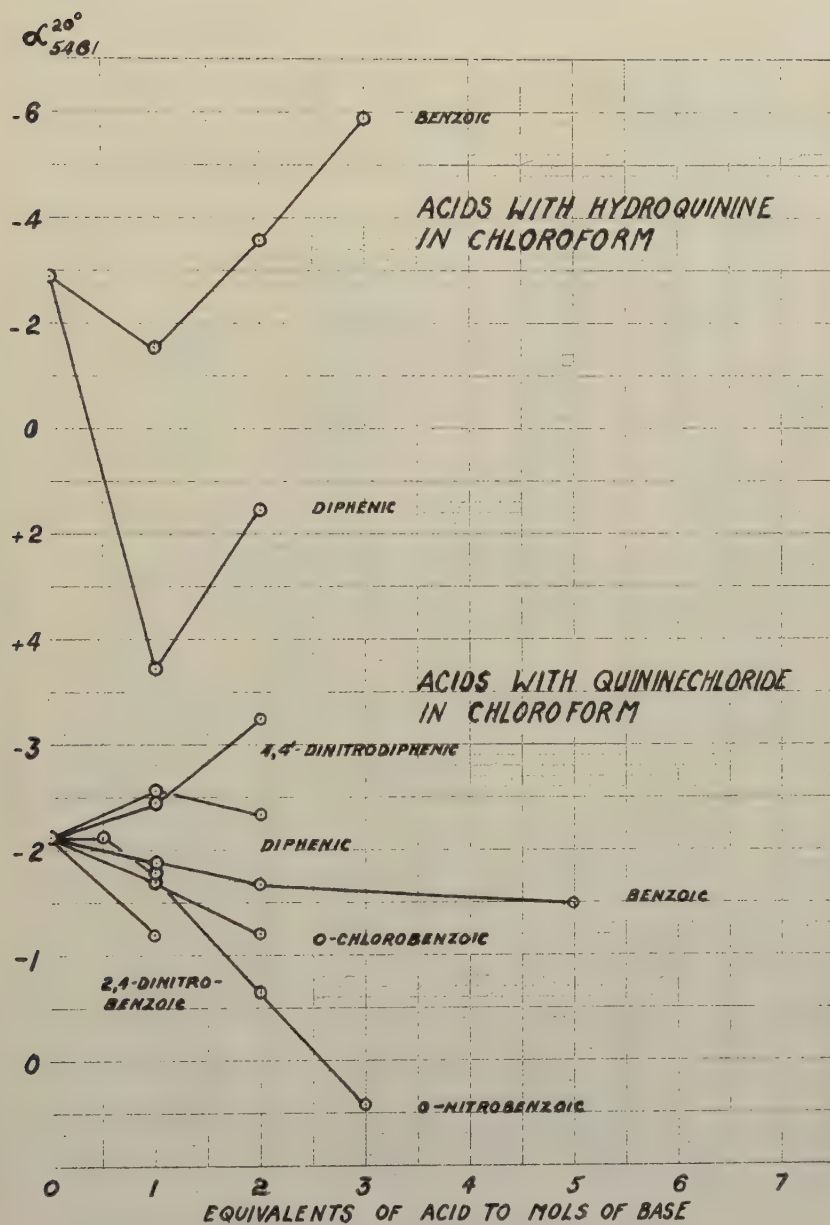
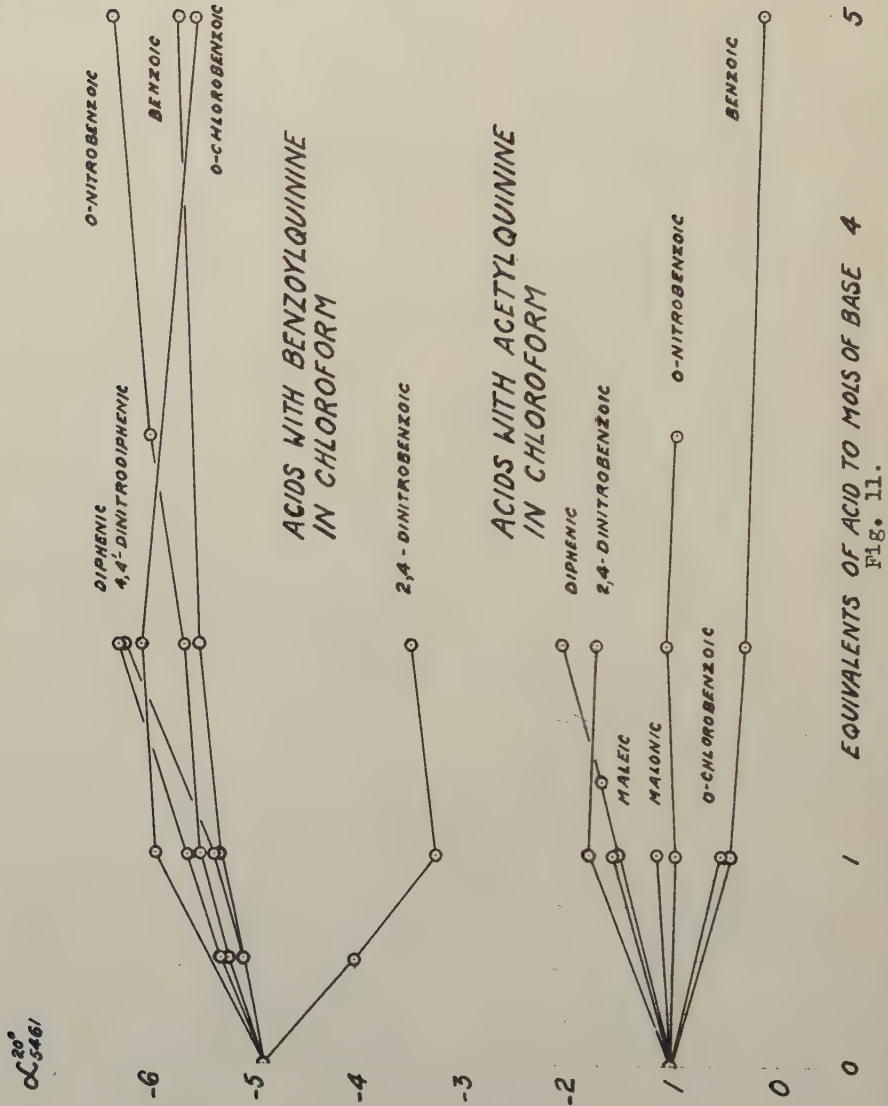


Fig. 10



4-Nitrodiphenic acid¹ was prepared from phenanthraquinone following Schmidt's² method with some modifications suggested by Werner's directions for nitration. The mononitration was carried out by boiling 30 g. of phenanthraquinone dissolved in 350 cc. of nitric acid (sp. gr. 1.42) for twenty minutes. The 4-nitrodiphenic acid was obtained by the oxidation of the 2-nitrophenanthraquinone.

4,4'-Dinitrodiphenic acid was prepared by the oxidation of 2,7-dinitrophenanthraquinone³, which in turn had been made by the use of Schmidt and Kämpf's method for the dinitration of phenanthraquinone. The acid was further purified by crystallization from boiling 30% acetic acid.

Bases.- The following bases were used and, when not available commercially, were prepared as described:

Quinine alkaloid, anhydrous, U. S. P. (Mallinckrodt) was used. This had a M. P. 172° and (α)_D²⁰ -134.2° for c = 1.2968 g in chloroform.

Hydroquinine was prepared by dissolving 6.5 g. of quinine in dilute sulphuric acid, adding about 0.3 g. of Raney's⁴ catalyst, and hydrogenating, at an initial pressure of three atmospheres, for twelve minutes. The catalyst was separated by filtration, and the filtrate made alkaline with sodium hydroxide. The precipitated hydroquinine was dissolved in benzene, dry hydrogen chloride passed into the solution, and the precipitated hydrochloride filtered off and dried. It melted at 232°. The free base was liberated by dissolving the hydrochloride in water and treating with sodium carbonate. After drying for an hour at 100°

¹Schmidt, Ber., 36, 3731 (1903).

²Werner, Ann., 321, 336 (1902).

³Schmidt and Kämpf, Ber., 36, 3739 (1903).

⁴Adkins and Covert, J. Am. Chem. Soc., 54, 1651 (1932)

it melted at 172° . The hydroquinine thus obtained did not decolorize potassium permanganate, which proved the absence of quinine as an impurity. $(\alpha)_D^{20^{\circ}} -143.8^{\circ}$ for $c = 2.4$ g. in 95 %¹ alcohol; the value given in the International Critical Tables is $(\alpha)_D^{20^{\circ}} = -142.2^{\circ}$.

Acetylquinine was prepared by the action of acetic anhydride on quinine at $60-80^{\circ}$ for several hours according to the directions of Hesse.² The product melted at $116-117^{\circ}$, which agreed with Seekles'³ observation. $(\alpha)_D^{20^{\circ}} = -27.0^{\circ}$ for $c = 1.4848$ g⁴ in 95 % alcohol; the value on the International Tables is $(\alpha)_D^{14.4^{\circ}} = -30.9^{\circ}$ for $c = 1$ g. in the same solvent.

Benzoylquinine was prepared according to the directions of Wunsch.⁵ The benzoylquinine so obtained melted at 129° and $(\alpha)_D^{20^{\circ}} = +119.3^{\circ}$ for $c = 1$ g. in absolute alcohol. Seekles⁶ gives the M. P. 138° and $(\alpha)_D^{19.2^{\circ}} = +119.9^{\circ}$.

Quininechloride⁷ was made according to the directions of Comstock and Königs except that quinine was used in place of quinine monohydrochloride. The base had a M. P. 151° and $(\alpha)_D^{15} = +59.1^{\circ}$ for $c = 1.966$ g. in absolute alcohol. The rotation obtained by Comstock and Königs was $(\alpha)_D^{15} = +61.0^{\circ}$.

Brucine, Eastman's practical, was purified by dissolving in chloroform and precipitating with dry ether. The precipitated brucine, dried at 100° for several hours, melted at 178° and

¹International Critical Tables," The McGraw Hill Book Co., New York, 1930, Vol. VII, p. 472.

²Hesse, Ann., 205, 315 (1880).

³Seekles, Rec. Trav. Chim., 42, 72 (1923).

⁴Op. cit., p. 472.

⁵Wunsch, Ann. Chim., (VII) 7, 126 (1896).

⁶Seekles, op. cit.

⁷Comstock and Königs, Ber., 17, 1988 (1884).

$(\alpha)_D^{20} = -120.5^\circ$ for $c = 1.5768$ g. in chloroform. Hilditch¹ gives $(\alpha)_D^{20} = -121$ for $c = 2.5$ g. in chloroform.

Morphine, of M. P. 252° and $(\alpha)_D^{23} = -131.1^\circ$ for $c = 2.292$ g. in absolute methyl alcohol was used. Schryver and Lees² give a M. P. 254° and $(\alpha)_D^{23} = -130.9^\circ$.

Betti's base (β -naphthol-phenyl-methylamine) was prepared according to the directions of Marvel and Hiers³. The free base resolved according to the directions of Betti⁴, gave $(\alpha)_D^{20} = +59.75^\circ$ for $c = 4.2664$ g. in benzene. Betti gives $(\alpha)_D^{20} = +58.84^\circ$ under the same conditions.

d-Betti's Schiff base (d-benzal- β -naphthol-phenyl-methylamine) was obtained by condensing d-Betti's base with benzaldehyde.⁵ For this material $(\alpha)_D^{20} = +109.0^\circ$ for $c = 0.7436$ g. in benzene; Betti gives $(\alpha)_D^{20} = +110.68^\circ$.

d-N-p-Dimethylaminobenzal- β -naphthol-phenyl-methylamine was made by condensing d-Betti's base with p-dimethylaminobenzaldehyde. The product has a M. P. 220° and $(\alpha)_D^{20} = +694^\circ$ for $c = 0.1900$ g. in benzene; Betti gives $(\alpha)_D^{20} = +704.21^\circ$.

d-N-p-Dimethylaminobenzyl- β -naphthol-phenyl-methylamine was obtained by hydrogenation of the above base suspended in benzene with Raney's catalyst. In three hours the Schiff base was in solution and the reduction complete. The filtered solution was evaporated in a stream of air, and the product, recrystallized from alcohol, melted at $139-139.5^\circ$. Two different reductions gave products with the following very nearly agreeing

¹Hilditch, J. Chem. Soc., **93**, 1388 (1908).

²Schryver and Lees, J. Chem. Soc., **77**, 1038 (1900).

³Marvel and Hiers, op. cit.

⁴Betti, Gazz. Chim. Ital., **36**, **II**, 392 (1906).

⁵Betti, ibid., **37**, **I**, 62 (1907).

⁶Ibid., **46**, **I**, 200 (1916).

rotations, $(\alpha)_{5461}^{20^\circ} = +268.8^\circ$ and $+266.2^\circ$ for $c = 0.1816$ g. in dry ether.

The hydrochloride was prepared by passing dry hydrogen chloride into an ether solution of the reduced base; M. P. 175° (dec.).

Anal. Calcd. for $C_{26}H_{28}NOCl_2$: Cl, 15.58

Found: Cl, 15.68 and 15.31 (Volhard)

Howard's base (β -naphthol- β -phenylethyl-methylamine)¹ was prepared according to the directions of Kharasch and Howard. The dry material melted at $108-109^\circ$ and did not exhibit the phenomena of liquid crystals as noted by Howard.

d- and l-Howard's base were obtained by resolution of the racemic mixture. Sixteen grams of the free base was added to the hot solution of 10 g. of tartaric acid (theory 8.66 g.) in 150 cc. of alcohol. On further heating a clear solution was obtained; almost immediately thereafter the precipitate of the tartrate began to form. After standing over night, the precipitate was filtered off, boiled for a few minutes with 100 cc. of alcohol containing 1 g. of tartaric acid, and cooled. The weight of the salt when dry was 10.14 g.; theory demands 12.33 g. The free base was liberated by treating the tartrate with a dilute solution of potassium hydroxide at 0° C. and extracting with ether. The dried ether extract, concentrated to a small volume, deposited 5 g. of crystalline d-base of M. P. 108° and $(\alpha)_{5461}^{20^\circ} = +187.5^\circ$ for $c = 1.1088$ g. in anhydrous ether.

On concentrating the combined alcoholic filtrates by evaporation in a stream of air, successive portions of solid salt were collected until approximately 5 g. had been obtained.

¹Kharasch and Howard, J. Am. Chem. Soc., 56, 1371 (1934).

The filtrate, now only 15 to 20 cc. in volume and quite syrupy, was evaporated further under a stream of air until it solidified. On liberating the base from this mixture of salt and tartaric acid, drying the ether extract, and crystallizing out the base, 4 g. of the l-form was obtained. This gave a M. P. 108° and $(\alpha)_{5461}^{20} = -198.8^{\circ}$ for $c = 1.1088$ g. in anhydrous ether.

Solvents.- In order to obtain reproducible results, especial care was taken to purify the solvents used:

Chloroform, U. S. P., was washed five times with distilled water to remove the alcohol, dried over anhydrous calcium chloride, and distilled. The constant boiling fraction was tested before use by taking the rotation of 0.3242 g. of quinine dissolved in 25 cc. using a 2 dm. tube. It was rejected if α_{5461}^{20} deviated more than 0.02° from -3.43° . Later the rotation of the mixture of 0.3242 g. of quinine and 0.1220 g. of benzoic acid was used as a test. For this solution $\alpha_{5461}^{20} = -2.87^{\circ}$.

Cellosolve, the monoethyl ether of ethylene glycol (Union Carbide), was distilled to obtain the constant boiling fraction.

Procedure.- To determine the rotation curve for a given acid and base pair the concentration of the base was maintained constant. In general 0.001 mols of base was used. This was weighed out into a 25 cc. volumetric flask and the acid added in proportion from 0.5 to 20 mols or the limit of solubility. The volume was made up with solvent to 25 cc. at 20° . Eight to ten readings with the empty polariscope tube in place were used to determine the zero. The tube was then filled with solution and the temperature brought to $20^{\circ} \pm 0.5^{\circ}$ by circulating water from the thermostat through the jacket of the tube. As a homogeneous light source a mercury arc was used with Corning filters No. 351, H. R. Yellow Shade Yellow and No. 512, Didymium, 5 mm. Eight to

ten readings were used to determine the rotation. In making readings the end point was first approached from one side and then the other. The readings were plotted using the angles of rotation as the ordinates and the ratios of equivalents of acid to mols of base as the abscissae.

Rotations.- The following rotations were obtained by the procedure outlined above.

Rotations of mixtures of 0.001 mols of quinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.001 mols of quinine, $\alpha_{5461}^{20^\circ} = -3.48^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Acetic Acid		Chloroacetic Acid		Phenylpropionic Acid	
0.705	-2.92	0.445	-3.29	0.50	-2.90
1.08	2.96	0.765	2.73	0.90	2.54
1.18	3.28	1.13	2.60	1.00	2.49
2.07	5.21	1.62	3.38	1.10	2.79
2.64	5.98	2.22	4.45	1.50	3.68
5.58	7.93	3.24	5.87	2.00	4.84
8.16	8.33	7.92	8.46	3.00	6.09
15.45	8.82	18.74	9.01	5.00	6.91
18.43	9.07			10.00	7.22
glacial	8.44			20.00	7.19
Lauric Acid		Trichloroacetic Acid		Palmitic Acid	
0.518	-3.14	0.329	-3.43	1.00	-2.92
1.01	2.98	0.606	3.23	2.00	5.08
2.02	5.75	1.14	2.80	5.00	7.25
5.00	7.04	2.01	3.25	10.00	7.81
10.00	7.70	4.13	6.61	15.00	7.83
....		8.66	8.62		

Mols Acid Mols Base	20° α 5461	Mols Acid Mols Base	20° α 5461	Mols Acid Mols Base	20° α 5461
Benzoic Acid		o-Phenylbenzoic Acid		o-Chlorobenzoic Acid	
0.50	-3.18	0.50	-3.32	0.512	-3.57
1.00	2.87	1.00	3.69	0.756	3.77
1.50	4.88	2.00	4.72	1.00	4.27
2.00	6.34			1.26	4.65
3.00	7.97			2.01	5.71
5.00	9.00			5.05	6.51
10.00	9.35			8.35	6.46
20.00	9.19				
Phenylacetic Acid		Crotonic Acid		Cinnamic Acid	
0.50	-2.70	0.50	-2.91	0.10	-3.17
1.00	2.13	1.00	2.50	0.50	-1.15
2.00	4.26	1.50	3.80	0.70	-0.18
3.00	5.58	2.00	4.89	1.00	+1.47
5.00	6.37	3.00	6.21	1.30	+0.09
10.00	6.81	5.00	7.19	1.50	-0.92
20.00	6.88	8.00	7.61	2.00	2.68
....		10.00	7.76	3.00	4.38
....		20.00	7.82	5.00	5.40
....				7.00	5.70
....				10.00	5.75
....				20.00	5.47
Anisic Acid		o-Nitrobenzoic Acid		2,4-Dinitrobenzoic Acid	
0.50	-2.41	0.50	-1.05	0.25	-1.78
1.00	1.28	0.75	-0.13	0.50	+0.45
1.50	2.73	1.00	+1.31	0.65	+2.25
2.00	4.47	1.50	+0.66	0.75	+4.35
2.50	5.43	2.00	-0.32	1.00	+6.39
3.00	6.62*	3.00	-2.33	1.50	+4.69
5.00	7.06*	5.00	-4.87	2.00	+2.46
....				2.50	+0.16
....				3.00	-1.64

*Twice observed reading for 0.0005 mol quantities.

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
o-Toluic Acid		m-Nitrobenzoic Acid		2,4,6-Trinitrobenzoic Acid	
0.50	-3.33	0.50	-1.78	0.25	-1.56
0.75	3.30	1.00	0.18	0.50	+0.99
1.00	3.45	1.50	2.04	0.60	+1.93*
1.25	3.81	2.00	3.93	1.00	+6.47*
1.50	4.33	3.00	6.79		
2.00	5.01	5.00	8.80		
3.00	5.72				
5.00	6.24				
11.00	6.42				
p-Toluic Acid		p-Nitrobenzoic Acid		Salicylic Acid	
0.50	-2.44	0.50	-1.16	0.514	-3.72
1.00	1.22	1.00	+1.80	0.76	4.04
1.50	3.12	1.50	-0.45	1.00	4.22
2.00	4.80	2.00	-2.88*	1.25	4.67
3.00	6.68			2.07	6.26
5.00	7.92			3.74	8.74
....				5.00	9.43
Anthranilic Acid		o-Iodobenzoic Acid		3,5-Dinitrobenzoic Acid	
0.50	-4.16	0.50	-3.77	0.50	+0.18
1.00	5.31	1.00	4.83	1.00	2.22
1.50	6.36	1.54	5.86	1.50	0.47
2.00	7.37	1.95	6.32		
3.20	8.35				
5.00	9.33				

*Trace undissolved.

Rotations of mixtures of 0.00025 mols of quinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2dm. tube at 20°.

0.00025 mols of quinine, $\alpha_{5461}^{20^\circ} = -0.81^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Oxalic Acid		Phthalic Acid		Malonic Acid	
0.25	-0.29	0.25	-1.07	0.25	-0.94
0.50	+0.44	0.50	1.18	0.50	0.99
0.75	+0.09	0.75	0.99	0.75	0.95
....				1.00	0.95
Diphenic Acid		Maleic Acid		4-Nitrodiphenic Acid	
0.25	+0.50	0.25	-1.03	0.25	+0.17
0.50	+1.38	0.50	1.06	0.50	0.95
0.75	+0.56	0.75	1.06	0.75	1.34
1.00	+0.19	1.00	1.10	1.00	1.69
1.25	-0.02			1.25	1.73
1.50	-0.12				
Adipic Acid		4,4'-Dinitrodiphenic Acid		Azelaic Acid	
0.25	-0.72	0.25	+0.11	0.254	-1.07
0.50	0.62	0.50	1.10	0.512	1.49
0.75	1.02	0.75	1.95		
1.00	1.28	1.00	2.33		
Sebacic Acid					
		0.25	-1.02		
		0.50	1.20		
		0.754	1.33		
		1.00	1.45		

Rotations of mixtures of 0.0000625 mols of quinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.0000625 mols of quinine, $\alpha_{5461}^{20^\circ} = -0.21^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
4,4'-Dinitrodiphenic Acid	
0.25	+0.01
0.50	0.27
0.75	0.45
1.00	0.68
1.25	0.54*
1.50	0.53**

*Trace undissolved.

**Undissolved part was filtered off.

Rotations of mixtures of 0.001 mols of quinine and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dm. tube at 20°.

0.001 mols of quinine, $\alpha_{5461}^{20^\circ} = -5.41^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
p-Nitrobenzoic Acid		Salicylic Acid		Phthalic Acid	
0.50	-6.17	0.50	-5.98	0.25	-5.57
1.00	6.83	1.00	6.67	0.50	5.85
1.50	6.93	1.50	6.65	0.75	6.03
2.00	6.94	2.00	6.68	1.00	6.14
3.00	6.88	3.00	6.68	2.00	6.23
5.00	6.75	5.00	6.63		

	$\frac{\text{Mols Acid}}{\text{Mols Base}}$ $\alpha^{20^\circ}_{5461}$
Glycollic Acid	
0.46	-5.40
1.24	5.87
2.20	5.89
3.80	5.91
5.61	5.89

Rotations of mixtures of 0.00025 mols of quinine and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dm. tube at 20°.

0.00025 mols of quinine, $\alpha^{20^\circ}_{5461} = -1.37^\circ$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha^{20^\circ}_{5461}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha^{20^\circ}_{5461}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha^{20^\circ}_{5461}$
o-Nitrobenzoic Acid		o-Chlorobenzoic Acid		Oxalic Acid	
0.50	-1.53	0.50	-1.46	0.25	-1.39
1.00	1.71	1.00	1.51	0.50	1.31
2.00	1.70	2.00	1.54	0.75	1.28
5.00	1.75	5.00	1.54	1.50	1.25
Malonic Acid		Adipic Acid		Diphenic Acid	
0.25	-1.42	0.25	-1.40	0.25	-0.51
0.50	1.41	0.50	1.43	0.50	0.15
0.75	1.46	0.75	1.41	0.75	0.36
1.00	1.47			1.00	0.43
....				1.50	0.65
....				3.00	0.97

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
o-Phenylbenzoic Acid		3,3'-Dicarboxydiphenyl		4,4'-Dinitro- diphenic Acid	
0.25	-1.30	0.25	-1.55	0.25	-0.41
0.50	1.28	0.50	1.63	0.50	+0.55
1.00	1.23	0.75	1.78	0.75	0.50
1.50	1.19	1.00	1.82	1.00	0.45
....				1.50	0.29
....				3.00	0.09
Phthalic Acid					
		0.25	-1.40		
		0.50	1.51		
		1.00	1.51		
		2.50	1.57		

Rotations of mixtures of 0.001 mols of hydroquinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.001 mols of hydroquinine, $\alpha_{5461}^{20^\circ} = -2.92^\circ$

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Benzoic Acid		Diphenic Acid	
1.00	-1.63	0.50	+4.51
2.00	3.66	1.00	1.49
3.00	5.96		

Rotations of mixtures of 0.001 mols of acetylquinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.001 mols of acetylquinine, $\alpha_{5461}^{20^\circ} = -1.01^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Nitrobenzoic Acid		2,4-Dinitrobenzoic Acid	
1.00	-0.43	1.00	-0.96	-1.00	-1.77*
2.00	0.31	2.00	1.06	2.00	1.70*
5.00	0.15	3.00	0.94		
Diphenic Acid		o-Chlorobenzoic Acid		Malonic Acid	
0.50	-1.51	1.00	-0.52	0.50	-1.13
0.67	1.68				
1.00	2.03				
Maleic Acid					
0.50			-1.53		

*Twice observed value for a 1 dm. tube.

Rotations of mixtures of 0.001 mols of benzolquinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.001 mols of benzoylquinine, $\alpha_{5461}^{20^\circ} = +4.88^\circ$

Mols Acid Mols Base	α^{20° 5461	Mols Acid Mols Base	α^{20° 5461	Mols Acid Mols Base	α^{20° 5461
Benzoic Acid		o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.00	+5.30	1.00	+5.91	0.50	+5.23
2.00	5.51	2.00	6.04	1.00	5.49
5.00	5.72	5.00	5.54	2.00	5.66
....				3.00	5.98
....				5.00	6.35
2,4-Dinitrobenzoic Acid		Diphenic Acid		4,4'-Dinitrodiphenic Acid	
0.50	+4.01	0.25	+5.24	0.25	+1.27*
1.00	3.25	0.50	5.62	0.50	1.33*
2.00	3.49	1.00	6.26	1.00	1.56*

*Values obtained using 0.00025 mols of base.

Rotations of mixtures of 0.001 mols of quininechloride and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.001 mols of quininechloride, $\alpha_{5461}^{20^\circ} = +2.17^\circ$

Mols Acid Mols Base	α^{20° 5461	Mols Acid Mols Base	α^{20° 5461	Mols Acid Mols Base	α^{20° 5461
Benzoic Acid		o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.00	+1.88	1.00	+1.75	0.50	+2.11
2.00	1.69	2.00	1.22	1.00	1.78
5.00	1.50			2.00	0.68
....				3.00	-0.38

Mols Acid Mols Base	20° α 5461	Mols Acid Mols Base	20° α 5461	Mols Acid Mols Base	20° α 5461
2,4-Dinitrobenzoic Acid		Diphenic Acid		4,4'-Dinitrodiphenic Acid	
1.00	+1.23	0.50	+2.58	0.50	+0.62*
....		1.00	2.35	1.00	0.82*

*Values obtained using 0.00025 mols of base.

Rotations of mixtures of 0.00025 mols of morphine and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dm. tube at 20° .

0.00025 mols of morphine, $\alpha_{5461}^{20^{\circ}} = -0.94^{\circ}$

Mols Acid Mols Base	20° α 5461	Mols Acid Mols Base	20° α 5461	Mols Acid Mols Base	20° α 5461
o-Chlorobenzoic Acid		o-Nitrobenzoic Acid		Phthalic Acid	
0.50	-0.87	0.50	-0.76	0.25	-0.91
1.00	0.82	1.00	0.65	0.50	0.85
2.00	0.69	2.00	0.63	1.00	0.81
5.00	0.71	5.00	0.61	2.50	0.80
Diphenic Acid			4,4'-Dinitrodiphenic Acid		
0.25	-0.88			0.25	-0.86
0.50	0.91			0.50	0.82
1.00	0.84			1.00	0.79
2.50	0.82			2.50	0.72

Rotations of mixtures of 0.001 mols of brucine and varying amounts of acid dissolved in 25 cc. of chloroform and taken in a 2 dm. tube at 20°.

$$0.001 \text{ mols of brucine, } \alpha_{5461}^{20^\circ} = -4.72^\circ$$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Chlorobenzoic Acid		Diphenic Acid	
1.00	-1.47	1.00	-1.76	0.50	-2.28
2.00	0.71	2.00	1.29	1.00	-0.04
3.00	0.61	3.00	1.10	1.50	+0.45
5.00	0.51	5.00	1.11		

Rotations of mixtures of 0.0005 mols of d-Howard's base and varying amounts of acid dissolved in 25 cc. of cellosolve and taken in a 2 dm. tube at 20°.

$$0.0005 \text{ mols of d-Howard's base, } \alpha_{5461}^{20^\circ} = +0.68^\circ$$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$
Acetic Acid		o-Nitrobenzoic Acid		Diphenic Acid	
0.74	+0.43	0.50	+0.24	0.25	+0.39
1.12	0.42	1.00	-0.02	0.50	0.29
1.51	0.31	2.00	-0.05	1.00	0.12
2.37	0.14	5.00	-0.07	2.50	0.10
8.74	-0.02				
glacial	-0.27				

Rotations of mixtures of 0.0005 mols of l-Howard's base and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dm. tube at 20°.

0.0005 mols of l-Howard's base, $\alpha_{5461}^{20^\circ} = -0.71^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
o-Nitrobenzoic Acid		o-Chlorobenzoic Acid	
0.50	-0.23	0.50	-0.32
1.00	+0.05	1.00	0.00
2.00	0.08	2.00	+0.08
5.00	0.08		
Phthalic Acid		4,4'-Dinitrodiphenic Acid	
0.25	-0.27	0.25	-0.20
0.50	0.10	0.50	+0.10
1.00	0.38	1.00	0.22
2.50	0.54	2.50	0.13

Rotations of mixtures of 0.000125 mols of d-N-p-Dimethylaminobenzal- β -naphthol-phenylmethylaniline and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.000125 mols of d-N-p-Dimethylaminobenzal- β -naphthol-phenyl-methylaniline, $\alpha_{5461}^{20^\circ} = +2.77^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.00	2.85	1.00	2.80
2.00	2.76	2.00	2.79
5.88	2.82		

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$
Diphenic Acid		4,4'-Dinitrodiphenic Acid	
0.50	+2.81	0.50	+2.83*
1.00	2.85*		

*Trace undissolved.

Rotations of mixtures of 0.00025 mols of d-N-p-Dimethylaminobenzyl- β -naphthol-phenyl-methylamine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.00025 mols of d-N-p-Dimethylaminobenzyl- β -naphthol-phenyl-methylamine, $\alpha_{5461}^{20^\circ} = +1.97^\circ$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Nitrobenzoic Acid	
0.50	+1.97	0.50	+1.57
1.00	2.05	2.00	2.03
2.00	2.03	3.00	1.78
5.00	1.91	5.00	1.96
Diphenic Acid		o-Chlorobenzoic Acid	
0.25	+1.92	1.00	+1.99
0.50	1.62	3.00	2.01
1.00	1.59*		

*Trace undissolved.

Rotations of mixtures of 0.0001 mols of d-Betti's base and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dm. tube at 20°.

0.001 mols of d-Betti's base, $\alpha_{5461}^{20^\circ} = +2.66^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Acetic Acid		o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.21	+2.93	5.00	+2.70	1.00	+2.77
6.04	2.90			5.00	2.83
28.23	2.58				
43.98	2.37				
glacial	2.84				
m-Nitrobenzoic Acid		2,4-Dinitrobenzoic Acid		Adipic Acid	
3.50	+2.78	1.00	+2.76	0.50	+2.64
....		3.00	2.76	1.00	2.58
....				1.50	2.54
Sebacic Acid		Phthalic Acid		4,4'-Dinitrodiphenic Acid	
0.50	+2.95	1.50	+0.63	0.50	+2.30
2.50	2.89	4.00	0.64	1.50	2.54
Diphenic Acid					
		0.50	+2.58		
		2.50	2.89		

Rotations of mixtures of 0.0005 mols of d-Benzal- β -naphthol-phenylaminomethane and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20°.

0.0005 mols of d-Benzal- β -naphthol-phenyl-methylamine,
 $\alpha_{5461}^{20^\circ} = +2.75^\circ$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha^{20^\circ}_{5461}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha^{20^\circ}_{5461}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha^{20^\circ}_{5461}$
o-Chlorobenzoic Acid		o-Nitrobenzoic Acid		Diphenic Acid	
1.00	+2.76	2.00	+2.75	0.50	+2.76*
2.00	2.75				

*Trace undissolved.

Summary

1. With respect to the validity of the Kuhn hypothesis for asymmetric rearrangement of the first kind, it has been shown:

(a) Without the assumption that acids like 2,4-dinitrobenzoic can be dissymmetrized (which is a radical departure from classical stereochemistry) asymmetric rearrangement of an acid is not demonstrated by an anomalous rotation of its quinine salt in chloroform.

(b) In certain solvents, such as cellosolve, anomalous rotations may be demonstrated for diphenic acid itself and diphenic acids with substituents in positions other than 6 and 6' if the proper base is chosen, e.g. quinine not morphine.

2. The anomalous behavior of quinine salts has been shown to be related to the presence of the free hydroxyl group in the quinine molecule.

3. The resolution of β -naphthol- β -phenyl-ethyl- methyl-amine, VI, into its d- and l- forms has been accomplished:

(α) $_{5461}^{20^\circ} + 187.5^\circ$ and -188.8° for $c = 1.1088$ g. in anhydrous ether.

